REMARKS

Claims 1-22 and 27 are pending in the subject application. The Examiner has withdrawn claims 6-8 and 20-22 as being drawn to a nonelected invention. Applicants have hereinabove amended claims 1, 6, 15 and 27 and canceled claims 3, 4, and 18 without disclaimer or prejudice to applicants' right to pursue the subject matter of these claims in the future. Support for the amendments to the claims may be found, *inter alia*, in the specification as follows: claim 1: page 10, lines 3-10, 13-15 and 19-29; claim 6: page 10, lines 24-26; claim 15: page 11, lines 5-12, 15-17 and 21-31; and claim 27: page 10, lines 3-10, 13-15 and 19-21. Upon entry of this Amendment, claims 1-2, 5-17, 19-22 and 27, as amended, will be pending and claims 1-2, 5, 9-17, 19 and 27, as amended, will be under examination.

Examiner Interview

Applicants thank the Examiner for his time and participation in the June 3, 2010 telephone interview with the undersigned attorney.

The January 6, 2010 Final Office was discussed with the Examiner in the June 3, 2010 telephone interview. Specifically, applicants' undersigned attorney discussed with the Examiner the differences between the Ganesh et al. reference cited in the January 6, 2010 Final Office Action and applicants' claimed invention. The Examiner indicated that he would take applicants' comments regarding Ganesh et al. under consideration and but was noncommittal to the points applicants made in the June 3, 2010 telephone interview.

Information Disclosure Statement

The Examiner indicated on page 3 of the January 6, 2010 Final Office Action that the listing of references in the specification is not a proper information disclosure statement. The Examiner indicated that unless such references have been cited by the Examiner on form PTO-892, they have not been considered.

In response, applicants intend to submit an Information Disclosure Statement to disclose the listing of references in the specification.

Withdrawn Rejections

The Examiner indicated that the rejection of claims 1-4 and 9-18 under 35 U.S.C. §112, first paragraph is withdrawn in view of applicants amendment to independent claims 1 and 15 to recite "wherein the inhibitor of RAGE is selected from the group consisting of an antibody, an antisense molecule, an RNAi molecule and catalytic nucleic acid".

Rejections Under 35 U.S.C. §103

The Examiner rejected claims 1-5, 9-19 and 27 under 35 U.S.C. §103(a) as allegedly unpatentable over Ganesh et al. (Hum. Mol. Genet. (2002)); in view of Yan et al. (Nature 1996), further in view of Lado et al. (Epileptic Disord. 2002).

In response, applicants respectfully traverse the Examiner's ground of rejection. Nevertheless, without conceding the correctness of the Examiner's ground of rejection, claims 1, 15 and 27 have been amended.

As discussed in the June 3, 2010 telephone interview and for the reasons set forth below, applicants respectfully disagree with the Examiner's characterization of Ganesh et al.

As an initial matter, claim 1 has been amended to recite, in relevant part, "A method for treating a subject either during or soon after a seizure, in order to reduce the extent of neuronal cell death in the hippocampus and/or cerebral cortex of the subject resulting the seizure...". Claim 15 has been amended to recite, in relevant part, "A method for inhibiting neuronal cell death which would otherwise result from a seizure in a subject predisposed to having a seizure...". Claim 27 has been amended to recite, in relevant part, "A method for treating a subject either during or soon after a seizure, in order to

reduce the extent of neuronal cell death in the subject resulting from the seizure...". As discussed with the Examiner in the June 3, 2010 telephone interview, and for the reasons set forth below, such an amendment helps clarify the differences between applicants' claimed invention and the Ganesh et al. reference.

Characterization Of Ganesh et al.

(1) *Ganesh et al. disclose that AGEs are specifically associated with neuronal Lafora Bodies*

On page 4 of the January 6, 2010 Final Office Action, the Examiner asserted that "The Ganesh reference teaches that advanced glycation endproducts (AGEs) are specifically associated with neurons in a mouse model of epilepsy...".

Applicants respectfully disagree with this characterization of Ganesh et al. Ganesh et al. disclose that "Lafora bodies, present both in neuronal and non-neuronal tissue, are positive for ubiquitin and advanced glycation end-products only in neurons, suggesting different pathological consequence for Lafora inclusions in neuronal tissue" (abstract). Ganesh et al. disclose on page 1252, second column, that "Neuronal Lafora Bodies were ubiquitin-positive (Fig. 3A-C), and also reacted with an antibody to advanced glycation endproducts (AGEP)(Fig. 3D,E)." Ganesh et al. disclose on page 1252, second column that "moreover, Lafora bodies of liver and muscle tissues did not react with anti-ubiquitin or anti-AGEP antibody (Fig. 3L,M,N), suggesting different pathological consequence for Lafora inclusions in neuronal tissues". **Therefore, applicants maintain that Ganesh et al. disclose that AGEs are specifically associated with neuronal Lafora bodies.** In this regard, it is clear from the disclosure of Ganesh et al. that not all neurons contain lafora bodies, as evidenced by the statement on page 1259 that "...the majority of degenerating neurons do not contain Lafora bodies and not all cells that contain lafora bodies degenerate...".

(2) *Ganesh et al. disclose that AGEs are specifically associated with Neuronal lafora bodies*

On page 5 of the January 6, 2010 Final Office Action the Examiner asserted that "Ganesh teaches that the human disease and animal model are characterized by cytoplasmic inclusions (Lafora bodies) present in neurons, including those of the hippocampus and cerebral cortex, which also co-express the AGEs" citing to page 1252, Results, paragraph 2.

As discussed with the Examiner in the June 3, 2010 telephone interview, it is not clear what the Examiner means by the recitation "which also co-express the AGEs". Such statement seems to imply that the neurons, which contain the Lafora bodies, also express AGEs. However, Ganesh et al. does not disclose anything about neurons separately co-expressing AGEs. As discussed above with regard to point 1, Ganesh et al. disclose that AGEs are specifically associated with Lafora bodies within neurons.

(3) *Ganesh et al. distinguished between neuronal cell death and neuronal dysfunction.*

On page 5 of the January 6, 2010 Final Office Action, the Examiner asserted that "Ganesh et al. discloses that the mouse model was characterized by extensive neuronal cell death in the hippocampus (p. 1252, Results, paragraph 4) and explicitly states that the Lafora inclusion may induce neurotoxicity through interaction between AGEs and the receptor for advanced glycation endproducts (paragraph spanning pp. 1259-1260)."

Applicants respectfully disagree with this characterization of Ganesh et al. Ganesh et al. disclose on page 1252, results, paragraph 4 that "Ultrastructural analysis in knockout mice revealed isolated or full rows of cerebellar Purkinje cells, hippocampal pyramidal and granular cells, and cerebral cortical pyramidal cells

showing unequivocal features of somatic degeneration as early as 2 months of age (Fig 4A-H)." Ganesh et al. go on to postulate at the paragraph spanning page 1259 to page 1260 whether Lafora bodies are toxic to neuronal cells. Ganesh et al. disclose "Since the majority of degenerating neurons do not contain Lafora bodies and not all cells that contain Lafora inclusions degenerate, the formation of Lafora bodies may not necessarily lead to neuronal cell death. However, a causative role for Lafora inclusion in neuronal dysfunction cannot be excluded". (emphasis added). **Thus, Ganesh et al. clearly distinguishes neuronal cell death and neuronal dysfunction.**

Ganesh et al. go on to disclose at the paragraph spanning pages 1259 to 1260 that "Inclusions harboring ubiquitin and/or AGEP modified proteins have been implicated in the pathogenesis of a number of degenerative diseases. Lafora inclusions may thus induce neuronal stress and neurotoxicity due to a diminished ubiquitin proteolytic system and/or by generation of reactive oxygen species through an interaction between AGEP and RAGE receptor for advanced glcyation end-products)" (emphasis added). Therefore, Ganesh et al. merely discloses that a causative role for Lafora inclusion in neuronal dysfunction cannot be excluded and one of the postulated mechanisms by which neuronal stress and neurotoxicity may be induced is the generation of reactive oxygen species through an interaction between AGEP and RAGE.

(4) *Ganesh et al. never suggest blocking the interaction between AGE and RAGE, let alone that blocking such interaction can reduce or inhibit cell death which results, or would have resulted from, a seizure.*

The Examiner states on page 5 of the January 6, 2010 Final Office Action that "Although the Ganesh reference strongly suggests that blocking the interaction between AGE and RAGE would be desirable for treating the neuronal damage in the cerebral cortex and hippocampus associated with this seizure disorder, the reference does not

explicitly teach administration of an inhibitor of RAGE either during or soon after a seizure to reduce the extent of neuronal damage, as claimed.

Applicants respectfully disagree with this characterization of Ganesh et al. Ganesh et al. make no disclosure that Lafora bodies lead to, or are associated with, neuronal cell death. In fact Ganesh et al. explicitly state on page 1259 that "the formation of Lafora bodies may not necessarily lead to neuronal cell death" and also states "the majority of degenerating neurons do not contain lafora bodies...". Moreover, Ganesh et al. do not disclose that Lafora bodies have a causative role in neuronal dysfunction, but merely that a causative role cannot be excluded and one of the postulated mechanisms by which neuronal stress and neurotoxicity may be induced is by the generation of reactive oxygen species through an interaction between AGEP and RAGE. Nowhere do Ganesh et al. ever suggest blocking the interaction between AGE and RAGE, let alone that blocking such interaction can reduce or inhibit cell death which results, or would have resulted from, a seizure. In fact, RAGE is mentioned only once in Ganesh et al. at page 1260.

Applicants' Claimed Invention

In contrast to Ganesh et al., applicants' claimed invention is directed to a method for treating a subject either during or soon after a seizure, in order to reduce the extent of neuronal cell death in the hippocampus and/or cerebral cortex of the subject resulting the seizure..." (Claim 1); "A method for inhibiting neuronal cell death which would otherwise result from a seizure in a subject predisposed to having a seizure..." (Claim 15); and "A method for treating a subject either during or soon after a seizure, in order to reduce the extent of neuronal cell death in the subject resulting from the seizure..." (Claim 27) (emphasis added).

For the reasons discussed in points (1) - (4) above, applicants maintain that Ganesh et al. do not disclose, or even suggest, that

blocking the interaction of AGE and RAGE would be desirable for reducing the extent of neuronal cell death.

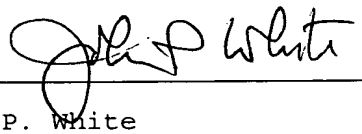
Applicants maintain that no combination of Ganesh et al. with Yan et al. and Lado et al. would render obvious applicants' claimed invention. Specifically, for the reasons discussed above in points (1) - (4), Ganesh et al. do not disclose or even suggest that neuronal cell death in the hippocampus and/or cerebral cortex which would otherwise result from a seizure can be reduced by administering a RAGE inhibitor, as recited in applicants' amended claim 1. Moreover, Ganesh et al. do not disclose or even suggest that neuronal cell death which would otherwise result from a seizure can be inhibited by administering a RAGE inhibitor. Yan et al. and Lado et al. do not overcome the deficiencies of Ganesh et al. As such, applicants' maintain that no combination of Ganesh et al. with Yan et al. and Lado et al. renders applicants' claimed invention obvious.

In view of the preceding remarks, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection under 35 U.S.C. §103

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fees, other than the enclosed $1,110.00 fee for a three-month extension of time and $810.00 fee for filing a Request For Continued Examination, is deemed necessary in connection with the filing of this Amendment and the RCE which it accompanies. A check in the amount of $1,920.00 is enclosed. If any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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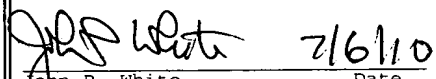

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